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10/534,290

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Toshiyuki Takasu

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2100 PENNSYLVANIA AVE. NW

WASHINGTON, DC 20037-3213

EXAMINER

RAE, CHARLESWORTH E

ART UNIT

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/534,290 | <b>Applicant(s)</b><br>TAKASU ET AL. |  |
|                              | <b>Examiner</b><br>CHARLESWORTH RAE  | <b>Art Unit</b><br>1611              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 November 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/26/08</u> .  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicant's arguments, filed 11/26/08, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

This action is made final. The finality of the action is necessitated by the claim amendment changing the scope of the invention.

### **Status of the Claims**

Claims 1-12 are currently pending in this application and are the subject of the Office action.

### **Claim Amendments**

Applicant's claim amendment, received 11/26/08, is acknowledged. Applicant's statement that no new matter has been added by amendment and statements pointing out where support may be found in the specification for the amendments are acknowledged and made of record (see applicant's Response, pages 4-5).

### **Priority Claim**

Applicant's statement that no sworn English translation of the priority document of the instant application has been filed with the Office is acknowledged and made of record. Thus, the effective filing date of the instant application for prior art purposes is the filing date of the instant application, which is 11/04/2003.

### **Information Disclosure Statement**

Applicant's information disclosure statement, received 11/26/08, has been considered and made of record.

## REJECTIONS

### ***Nonstatutory Obviousness-Type Double-Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**Claims 1-12 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over reference claims 1-12 of U.S. Patent 6,346,532 ('532), in view of Ladouceur et al. (U.S. Patent 6,699,860), and in further view of Akaha et al. (JP 2001114736; already made of record).**

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims. In particular, reference claim 6 is drawn in part to the instant claimed compound: (R)-2-(2-aminothiazol-4-yl)-4'[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide. Unlike the instant claims, the reference claims are directed specifically to compounds and compositions encompassing the same instantly claimed compounds.

The below discussions of Ladouceur et al and Akaha et al. are incorporated by reference. Ladoucer et al. teach methods of treating urologic disorders (e.g. incontinence) comprising administering a beta-3 agonist drug and Akaha et al. teach beta-3 agonist drugs for treating various conditions, including pollakisuria and urinary incontinence (abstract).

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In spite of the difference between the instant claims and the reference claims, it would have been obvious to a person of skill in the art at the time the invention was made to arrive the instant claimed invention in view of the reference claims and the prior art. One would have been motivated to combine the reference claims with the teaching to treat a patient with a urologic disorder (e.g. incontinence, pollakuria) since the reference claims and the instant claims are directed to the same compounds, which are beta-3 agonist drugs, and Ladoucer et al. and Akaha et al. suggest that beta-3 agonists drugs are useful for treating urologic conditions (e.g. incontinence, pollakiuria), Thus, the instant claims are deemed to be an obvious variant of the reference claims in view of the prior art.

#### **Claim rejections – 35 USC 103(a) – Newly applied**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1-4, 6-9, and 11-12 are rejected under 103(a) as being unpatentable over Maruyama et al. (WO99/20607; equivalent English translation U.S. Patent 6,346,532 B1), in view of Ladouceur et al. (U.S. Patent 6,699,860).**

Maruyama et al. teach beta-3 agonist drugs that are selective to beta-3 receptor in human beings (col. 1, lines 59-67). Maruyama et al. teach that beta-3 agonist are useful for treating obesity, hyperglycemia, and hyperlipidemia (col. 2, lines 1-37). Maruyama et al. teach compounds that are isolated and purified as a free compound, or a salt thereof (col. 9, lines 34-42). Maruyama et al. teach (R)-2-(2-aminothiazol-4-yl)-4'[2-(2-hydroxy-2-phenylethyl)-amino]-ethyl]-acetanilide dihydrochloride (applicant's elected compound; see reference claim 6 and col. 19, Example 36). Maruyama et al. teach compounds for intravenous injection in doses of around 0.001 mg/kg to 10 mg/kg per day in single or divided doses (col. 12, lines 20-29).

However, Maruyama et al. do not teach applicant's claimed overactive bladder population.

Ladouceur et al. teach beta-3 agonists are useful in the treatment of beta-3 mediated conditions, including hyperglycemia (diabetes), obesity, gastrointestinal disorders, neurogenic inflammation, ocular hypertension, and in the treatment of **urological disorders**, including benign prostatic hyperplasia and incontinence (col. 1, lines 30-54; col. 202, lines 31-67). Ladouceur et al. state that the amount of active ingredient to be administered in the treatment of a beta-3 mediated condition can vary widely according to such considerations as the particular compound, dosage unit employed, the mode of administration, the period of treatment, the age and sex of the patient treated, and the nature and extent of the condition treated (col. 205, lines 4-10).

It would have been obvious to a person of skill in the art at the time the invention was made to combine the cited references to treat a human subject with a urologic disorder (e.g. incontinence, benign prostatic hyperplasia) comprising administering to said human subject in need thereof the instant claimed compound as taught by Maruyama et al. to control the urologic symptoms. One would have been motivated to do so because Ladouceur et al. suggest that beta-3 agonists may be useful in treating urologic disorders (e.g. incontinence and benign prostatic hyperplasia) and incontinence is a known symptom of overactive bladder. Also, Maruyama et al. teach beta-3 agonists compounds, including applicant's claimed compound, that have a selective stimulating action to human beta-3-receptor such that one would expect to treat a human suffering with incontinence as taught by Ladoucer et al. with a compound taught by Maruyma et

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al. since Maruyama et al. teach beta-3 agonists drugs that are selective for beta-3 human receptors (col. 11, line 56 to col. 12, line 11) and Ladouceur et al. teach beta-3 agonist drugs to treat incontinence in humans (col. 1, lines 30-54; col. 202, lines 31-67). Besides, Maruyama et al. and Ladouceur et al. are both concerned with treating conditions mediated by beta-3 agonist receptors with beta-3 agonist drugs.

Regarding claims 2 and 7, Ladouceur et al. teach urological disorders, including benign prostatic hyperplasia (col. 1, lines 30-54; col. 202, lines 31-67).

Regarding claims 3-4 and 8-9, Ladouceur et al. provides a general teaching of urologic disorders and exemplifies incontinence (col. 1, lines 30-54; col. 202, lines 31-67) such that one would reasonably expect to successfully treat any urologic disorder mediated by beta-3 agonist receptors in human subjects, including applicant's claimed urinary urgency and urinary urge incontinence, since both Ladouceur et al. and Maruyama et al. teach beta-3 agonist drugs selective to human beta-3 receptors and Ladouceur et al. teach that beta-3 agonist drugs are useful for treating urologic disorders (e.g. incontinence). Further, one would reasonably expect that a subject with urinary incontinence would also experience at least some urinary urgency and at least some urinary urge incontinence absent evidence to the contrary.

Regarding the term "free base form" as recited in claim 6, Maruyama et al. teach compounds that are isolated and purified as a free compound (col. 9, lines 34-42).

Regarding claims 11 and 12, Maruyama et al. teach beta-3 agonist drugs that are selective to beta-3 receptors in human beings and therefore one would reasonably expect to treat a human subject suffering with a urologic disorder (e.g. incontinence) as

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taught by Ladouceur et al. with a compound of the prior art since the compounds taught by Maruyama et al. are selective to the beta-3 receptors in human beings (col. 10, lines 7-10).

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

**Claims 5 and 10 are rejected under 103(a) as being unpatentable over Maruyama et al. (WO99/20607; equivalent English translation U.S. Patent 6,346,532 B1), in view of Ladouceur et al. (U.S. Patent 6,699,860), and further in view of Akaha et al. (JP 2001114736; already made of record).**

The above discussions of Maruyama et al. and Ladouceur et al. are incorporated by reference. These references do not teach pollakiuria.

Akaha et al. teach beta-3 agonist drugs for treating various conditions, including pollakisuria and urinary incontinence (abstract).

It would have been obvious to a person of skill in the art at the time the invention was made to treat a human subject with pollakiuria as taught by Akaha et al. with a beta-3 agonist drug as taught by Maruyama et al. One would have been motivated to do so because Ladouceur et al. suggest that beta-3 agonist drugs are useful for treating urologic disorders and Akaha et al. also teach beta-3 agonist drugs to treat pollakiuria. Besides, Maruyama et al., Ladouceur et al. and Akaha et al. are all concerned with methods of treatment comprising beta-3 agonist drugs and both Ladouceur et al. and Akaha et al. teach urinary incontinence.

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

### **Response to applicant's arguments**

Applicant's arguments with respect to the rejection under 103(a) have been considered but are moot in view of the new ground(s) of rejection. The merits of Maruyama et al. is maintained.

Applicant's argument that the claimed invention shows unexpectedly superior effects in efficacy when compared to known agent for treating overactive bladder is not found to be persuasive because the instant claims are not commensurate with the scope of the exemplified data. First, the instant claims do not recite a dose amount; however, applicant discloses that intravenous administration of compound A did not affect bladder contraction pressure until the dose 3 mg/kg and that the effects of compound A is dose-dependent (specification page 21, especially second full para.). Hence, applicant's claim of unexpected superior results would not reasonably include doses of compound A of less than 3 mg/kg.

Second, applicant's assertion that compound A is superior for treating overactive bladder disorders when compared to CGP 12,177A is not supported by the exemplified data since applicant has not compared the effects of CGP 12,177A and compound A on micturition (see page 27 and Figures 3-5). Besides, although applicant's carbachol study data do suggest that compound A possesses superior antagonistic effects on smooth muscle relaxation when compared to CGP 12,177A, which is also a beta-3

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agonist drug (specification, page 3, lines 1-4; and pages 18-20, Tables 1-4 and Figures 1-2), applicant has not provided any objective evidence to show that the drug concentrations used in the carbachol studies correlate with the dose amount of compound A or CGP 12,177A that is effective in controlling micturition in the cyclophosphamide-induced overactive bladder rat model (see Figures 1-5). Hence, the superior results observed with the carbachol testing cannot be reasonably or predictably extrapolated to determine the effects of compound A or CGP 12,177A on micturition in the cyclophosphamide-induced overactive bladder model disclosed by applicant (page 27, and Figures 3-5).

#### **Relevant Art of Record**

The below art made of record and relied upon are considered pertinent to applicant's invention.

Cruz et al. (US Patent 6,630,515) is added to show the general state of the art teach that the clinical term "overactive bladder" is used generally to denote any form of incontinence characterized by increased frequency of micturition or desire to void, whether complete or episodic, and where loss of voluntary control ranges from partial to total (col. 1, lines 34-39). Cruz et al. teach that "urge incontinence" is the involuntary loss of urine associated with an abrupt and powerful desire to void, which is usually, but not always, associated with the urodynamic finding of involuntary (uninhibited) contractions of the detrusor muscle (col. 1, lines 39-44). Cruz et al. teach that a large

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subset of patients with uninhibited detrusor have some sort of neurologic impairment, in which case the clinical term is "detrusor hyperreflexia (col. 1, lines 45-57).

Skolnick (US Patent Application Pub. No. 2008/0009538; post art reference) teach the most widely used drug treatment for overactive bladder employs antimuscarinic agents, such as oxybutynin (para 0007). Overactive bladder can involve both peripheral and central control defects, including hypersensitivity of sensory neurons of the bladder (e.g., arising from inflammatory conditions, hormonal imbalances, or prostatic hypertrophy), destruction of the sensory nerve fibers, and damage to the spinal cord or brain stem causing interruption of transmitted signals (para 0006). Neurogenic overactive bladder (or neurogenic bladder) is caused by detrusor hyperreflexia secondary to neurologic disorders such as stroke, Parkinson's disease, diabetes, multiple sclerosis, peripheral neuropathy, or spinal cord injury (para 0006). Non-neurogenic overactive bladder is caused by detrusor muscle instability, arising from non-neurological abnormalities such as bladder stones, muscle disease, urinary tract infection and pharmacological side effects (para 0006). Despite pharmacological advances, there are still no satisfactory treatments for urinary incontinence and associated conditions caused by disorders of the lower urinary tract. Accordingly, there remains an important, unmet need for alternative compositions and methods to treat urinary incontinence and associated conditions caused by neurogenic and non-neurogenic overactive bladder, interstitial cystitis, prostatitis, prostatic hyperplasia, and other lower urinary tract disorders in mammalian subjects.

## **Conclusion**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

19 March 2009

/C. R./ Examiner, Art Unit 1611

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611